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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,904	02/17/2004	Lorraine D. Butlin	ISA-047.02	7556

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EXAMINER	
MAASHO, KERIMA K	

ART UNIT	PAPER NUMBER
1645	

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08/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/780,904	BUTLIN ET AL.	
	Examiner	Art Unit	
	Kerima Maasho	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16 and 18-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-39* is/are rejected.

7)☒ Claim(s) *15 and 16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*. See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed on 05/15/2007 has been entered into record. Claims 15-16, 18-39 are pending in the continued examination.

The text of those sections of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Claim Objections

1. Claims 15 and 16 are objected to because of the following informalities: The claims lack antecedent in the specification for the claimed anti-FSH monoclonal antibody as expressed by hybridoma cell line 00034004 and ECACC 00034005. These claimed cell lines could not be found in the specification. The cell lines deposited in the ECACC in accordance with the provisions of the Budapest treaty 1977 are ECACC 00032004 and ECACC 00032005 as recited in the specification. This appears to be a typographical error. Appropriate correction is required. The claims will be allowable once the objection is overcome.

Response to Arguments

Rejection/Objections Maintained

Applicants arguments filed 05/15/2007 have been fully considered but they are not persuasive.

Claim objection

2. Applicants traverse the objection to claim 22 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, Applicants assert the antibody pairs of claim 21 "may recognize different regions of the same antigen".

Claim 21 as amended still does not overcome the objection of claim 22 because as the examiner pointed out in the previous office action, even if the second antibody pair has a different specificity to at least one form of the combined alpha and beta chains of FSH from the first antibody pair, this does not preclude the first antibody from measuring total FSH in the sample (see page 5 of the previous office action). Because total FSH is accomplished through detecting the combination of FSH alpha and beta chains through binding of one antibody to the alpha subunit and another antibody of the antibody pair to the beta subunit the amendment of claim 21 with "at least one form" of the combined alpha and beta form... does not overcome the objection of claim 22 of not further limiting claim 21.

If Applicants intend for one of the pairs of antibodies recited in claim 21 not to bind total FSH based upon binding both the alpha and beta subunits, then this embodiment is not clearly set forth in the claims. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself.

The rejection is maintained for reasons of record and responses set forth above. Applicants' traversal is not commensurate in scope with the instantly claimed invention as claimed.

Claim Rejections - 35 USC § 102

3. ***Claim Rejections*** - 35 USC § 102(b): Claims 18, 26, 31,38 rejected under 35 U.S.C. 102(b) as being anticipated by Alffhan et al (1996) (see office action mailed on 11/15/2006).

Response to Applicants argument:

Applicants traverse the rejection to claims 18, 26, 31, and 38 under 35 USC 102(b) over Alfthan et al (1996) on the grounds that Afthan et al do not teach or suggest two assays using different antibody pairs directed against a different form of the gonadotropin. Applicants argue that Alfthan et al disclose at page 109 and 111 assays that use one pair of antibodies to distinguish among forms of hCG.

Alfthan et al disclose the use of a highly specific and ultrasensitive assay system to measure the concentrations of hCG and hCGβ in urine and serum samples using antibody pairs by comparing values for hCG and hCGβ (see abstract, Fig 1 and 2 and previous office action). On page 109, Alfthan et al teach the differential detection of hCG and hCGβ by using paired antibodies, as such the measurement for hCG and hCGβ are portrayed in Fig 1 on page 112. Therefore, Alfthan et al disclose first and second antibody pairs that bind to two different forms of hCG and based upon comparison

between these values, menopausal status can be determined. The rejection is maintained for reasons of record and responses set forth herein.

4. ***Claim Rejections*** - 35 USC § 102(e): Claims 18, 26, 31-32 and 38 rejected under 35 U.S.C. 102(e) as being anticipated by Birken et al (2003) (see office action mailed on 11/15/2006).

Response to Applicants argument:

Applicants traverse the rejection to claims 18, 26, 31-32 and 38 under 35 USC 102(e) over Birken et al (US Pat. 6,521,416) on the grounds that Birken et al do not teach or suggest using the compared results of the assay or the relative abundance of the forms to determine the menopausal status of the female.

It is the position of the examiner that Birken et al disclose the instantly claimed invention directed to a method of testing a human female individual to determine menopausal status, the method comprising two assay that employ tow antibody pairs directed to different forms of the gonadotropin (see col. 8, Figures 15 A-C, two assays, the first being for hLH concentration (figure 15C) and the second being a different form of hLHBcf which is dependent upon menopausal status (see Figure 15 A (perimenopausal, col. 8, lines 26-43), the antibody being specific for a protein portion and a carbohydrate moiety (see col. 10, lines 33-35; see sandwich format assays hLHBcf: col. 4, lines 40-5151; hLH: two different IRMAs (see col. 6, lines 62-63), IRMA are sandwich assays; Figure 8; also col. 9, lines 50-55; assay results were discernibly different from each other (see Figure 17 A-B and col. 8, lines 45-52 "no pattern match"; "typical postmenopausal concentrations of the hLHBcf'; col. 13, lines 50-

56 differences in hLH and hLHBcf (increased 6X-7X); the detection/determining was from the formation of color (see col. 9, lines 64-67 "enzyme, dye" produce color indications in assays).

Birken et al still anticipates the instantly claimed invention as now claimed.

5. ***Claim Rejections*** - 35 USC § 102(b): Claim 39 rejected under 35 U.S.C. 102(e) as being anticipated by O'Daly et al (2003) (see office action mailed on 11/15/2006).

Response to Applicants argument:

Applicants traverse the rejection to claims 39 under 35 USC 102(b) over O'Daly et al (US patent 5,391,272) on the grounds that O'Daly et al do not teach or suggest a device that can assay two forms of the same gonadotropin, wherein the relative abundance of the first and second forms of the same gonadotropin is dependent upon the menopausal status of the female.

O'Daly et al disclose a device for an immunoassay method that covers the claimed three configurations as pointed out in the previous office action. These are sample-receiving device, with a first and second signal producing means. O'Daly et al disclose a dual analyte detection immunosensor. Moreover, O'Daly et al suggest that the immunosensor may also be adapted to detect two analytes in a single step by using different enzymes conjugated to the analyte-binding agents. O'Daly et al teach the use of this system to determine analytes. The analytes could be any of a number of polypeptides including hormones such as follicle stimulating hormone (FSH) and

Luteinizing hormone (LH). As applicants point out the device is not specifically designed for the determination of the menopausal sate of a female, however the claimed device as claimed reads on O'Daly et al's invention that can utilize a number of monoclonal antibodies in an immunoassay.

O'Daly et al's teaching states: "All of the compositions and methods disclosed and claimed herein can be made and executed without undue experimentation in light of the present disclosure. While the compositions and methods of this invention have been described in terms of preferred embodiments, it will be apparent to those of skill in the art that variations may be applied to the composition, methods and in the steps or in the sequence of steps of the methods described herein without departing from the concept, spirit and scope of the invention. More specifically, it will be apparent that certain agents which are both chemically and physiologically related may be substituted for the agents described herein while the same or similar results would be achieved. All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the spirit, scope and concept of the invention as defined by the appended claims."

Therefore, O'Daly et al anticipate the claimed invention thus the rejection is maintained for reasons of record and responses set forth herein.

Claim Rejections - 35 USC § 103

6. ***Claim Rejections*** - 35 USC § 103(a): Claims18-23, 24, 26-28, 29, 38, 33-37 and 39 rejected under 35 U.S.C. 103(a) as being obvious over Berger et al (1988) in view of Bartoli (EP 0736771 A1, 1995) (see office action mailed on 11/15/2006).

Response to Applicants argument:

Applicants traverse the rejection of claims 18-23, 24, 26-28, 29, 38, 33-37 and 39 under 103(a) as being obvious over Berger et al (1988) in view of Bartoli (EP 0736771 A1, 1995) on the grounds that the teachings of Berger et al and Bartoli combined do not teach the claimed inventions.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., how the FSH forms disclosed in Berger would correlate with menopausal status) are not recited in the rejected claim(s). Applicants argue that the novel aspect of their invention is that comparative levels or relative abundance of two forms of the same gonadotropin may be detected by certain antibodies and may be correlated to and used to determine menopausal status. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns,* 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims do not recite any specific forms, just different forms, and EP0736771 teaches how to correlate the determination of hFSH with menopausal status. It is also the position of the examiner that Berger teaches changes in gonadal axis result in elevated or decreased FSH levels are known (see page 2351, col. 1, last paragraph) and characterizes the antigenic epitopes with a panel of antibody pairs which define combinations of reagents for mapping/characterizing and determining the presence or absence of hFSH associated with changes in hFSH levels in a biological samples and EP 0736771 Bartoli teaches

hFSH, to be a clinical marker for diagnosing a woman with menopause (see title, figure, abstract) and Bartoli provides teaching, guidance for the evaluation of biological samples for determining specific changes in hFSH levels associated with menopausal status.

Therefore, the claimed invention is still obviated by the combined teachings of Berger et al in view of Bartoli and the rejection is maintained.

7. Applicants traverse the rejection of claims 25 and 30 as being obvious over Berger et al, in view of Bartoli and further in view of Dullien (US Pat. 6,174,665).
It is the position of the examiner that Berger in view of Bartoli do teach a method of determining the menopausal status of a female individual, the sample evaluated is not from a female undergoing a course of hormone replacement therapy (HRT). Dullien teaches and shows the measurement of hFSH in a sample obtained from female human individual undergoing hormone replacement therapy in an analogous art for the purpose of monitoring hormone replacement therapy for effectiveness in alleviating symptoms associated with menopausal status (see previous office action).

It is the position of the examiner that the combined teachings of Berger et al, Bartoli and Dullien still obviate the claimed inventions as claimed, therefore the rejection is maintained.

Conclusion

All Claims remain rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kerima Maasho whose telephone number is 571-270-3055. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kerima K. Maasho

/Kerima Maasho/
Patent Examiner

/Jennifer Graser/
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